Remarks

Applicant appreciates the thorough examination of the present application as evidenced by the Final Office Action mailed May 21, 2003.

Claims 1, 14-21, and 31-51 are pending in the present application. Claims 16-19, 21, and 45-49 have been withdrawn from consideration. Claims 1, 14, 15, 20, 31-44, and 50-51 stand rejected.

I. Interview Summary

Applicant and the Applicant's representatives, Kenneth D. Sibley and Shawna Cannon Lemon, appreciated the opportunity to speak with the Examiner on June 6, 2003. During this telephonic interview, the Examiner was introduced to the inventor of the claimed invention, Dr. Richard C. Boucher, Jr. As the Examiner may recall, Dr. Boucher has extensive experience in pulmonary and critical care medicine. Dr. Boucher received a B.A. from Yale University in New Haven, Connecticut and an M.D. from Columbia University College of Physicians and Surgeons in New York, New York. Dr. Boucher also participated in a residency program at Columbia Presbyterian Hospital in New York, New York and served as a fellow at Royal Victoria Hospital in Montreal, Canada. Dr. Boucher is currently a Professor of Medicine and the Director of the Cystic Fibrosis/Pulmonary Research and Treatment Center at the University of North Carolina at Chapel Hill School of Medicine, where he holds an endowed chair as a William Rand Kenan Professor. Dr. Boucher is also a recipient of the Doris Tulcin and Paul Di Sant'Agnese Cystic Fibrosis Research Awards.

As noted by the Applicant during the telephonic interview to discuss primarily other pending cases before the Examiner, Applicant hereby provides the following response to address the Examiner's concerns regarding the above-referenced case.

II. Rejection Under 35 U.S.C. § 102

Claims 1, 15, 31-36, 42-44, and 50-51 stand rejected under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 5,863,563 to Scheele (Scheele) for the reasons set forth in the prior Office Action mailed November 13, 2002 (November Action).

The November Action asserts that "Scheele teaches a method of treating a patient with cystic fibrosis comprising causing the patient to inhale a composition comprising potassium bicarbonate. See, particularly, claims 1, 4, and 6." November Action, page 2. Applicant respectfully traverses this rejection.

Applicant concurs with the Examiner's assertion that "the mere recitation of a newly discovered function or property, inherently possessed by thing in the prior art, does not cause a claim drawn to those things to distinguish over the prior art." Final Office Action, page 3 (*quoting In re Swinehart,* 169 USPQ 226, 229 (CCPA 1971). However, this is not the case with respect to the claims of the present application.

The present invention relates to a method for treating chronic obstructive pulmonary disease, comprising administering at least one osmotically active compound to an airway surface in an amount effective to increase the volume of liquid on the airway surface wherein the at least one osmotically active compound comprises at least one salt, as recited in claim 1. In contrast, claim 1 of Scheele recites as follows:

> A method for treating the symptoms of a pulmonary condition involving **insufficient secretion of surfactant by type II alveolar cells**, said insufficiency being attributable to abnormally low pH of the aqueous film bathing the alveolar luminal surface of said cells, said method comprising causing a patient suspected of having said pulmonary condition to inhale an amount of a **pH-raising buffer** effective to alleviate said symptoms, wherein (1) the buffer is provided to the patient in the form of a powder, and (2) said pulmonary condition is selected from the group consisting of cystic fibrosis, pulmonary edema, bronchiectasis, bronchiolitis, bronchopneumonia, viral pneumonia, and encephalitis with retained secretions.

Clearly, the method of treating chronic obstructive pulmonary disease using, among other things, at least one osmotically active compound wherein the at least one osmotically active compound comprises at least one salt to alter the volume of liquid on the airway surface as disclosed in the present invention is not equivalent to the administration of a pH-raising buffer to increase the rate of surfactant by type II alveolar cells as proposed by Scheele. Consequently, Scheele does not describe the methods of the present invention, and thus, Scheele does not inherently possess the functions and/or properties of the present invention.

Applicant further notes that the teachings of Scheele do not accurately describe the relationship between pH, type II alveolar cells, and surfactant secretion. At column 1, line 51 through column 2, line 15, Scheele proposes an invention based on the alleged discovery that the pulmonary dysfunction characteristic of certain disease states is attributable to the inhibition of secretion of surfactant and other secretory molecules normally produced by type II alveolar cells. Scheele further proposes that this inhibition of secretion is believed to be caused by the uncoupling of endocytosis and exocytosis in these cells, as a result of an abnormally low pH at the apical surface, in the alveolar microenvironment. Scheele proposed that the abnormally low pH ultimately leads to a decrease in the elastic properties of pulmonary tissue, a concomitant decrease in the rate of gas exchange within the alveolus, and an overall decrease in pulmonary function resulting in development of a pulmonary disease syndrome.

In contrast to the assertions set forth in Scheele, McShane et al., Airway surface pH in subjects with cystic fibrosis. *Eur. Respir. J.* **21(1):**37-42 (2003) (a copy of which is enclosed) concludes that airway surface pH does not differ between cystic fibrosis and noncystic fibrosis subjects and further concludes that the cystic fibrosis transmembrane conductance regulator may not play a role in airway surface pH *in vivo*. Moreover, Scheele does not recognize or address the utility of increasing the **volume** of fluid in the airways in order to alleviate the problems resulting from the retained mucous secretions associated with chronic obstructive pulmonary diseases as noted in the present application. As such, Scheele does not represent an "old and well known method" and does not represent an "old and well known ultimate utility" as alleged in the Final Office Action, page 4.

Applicant further notes that the cited reference **must be enabling**, thereby placing the allegedly disclosed matter in the possession of the public. *See In re Brown*, 329 F.2d 1006, 1011, 141 U.S.P.Q. 245, 249 (C.C.P.A. 1964). Applicant respectfully submits that Scheele not only fails to provide the claim recitations of the present application, but also fails to provide an enabling disclosure to arrive at the present invention. As noted above, Scheele erroneously sets forth proposals regarding

the relationship between pH, type II alveolar cells, and surfactant secretion. Such erroneous propositions do not serve as an enabling, anticipatory reference.

Applicant further submits that one of ordinary skill in the art would not rely upon the proposals of Scheele directed toward using a pH-buffer effective to raise the pH of the aqueous fluid in the luminal microenvironment of the type II alveolar cells for the purpose of increasing surfactant secretion by type II alveolar (See Col. 2, lines 23-30) in order to arrive at a method comprising, among other things, administering at least one osmotically active compound wherein the at least one osmotically active compound comprises at least one salt to an airway surface of the subject in an amount effective to increase the volume of liquid on the airway surface. As noted above, the method disclosed in the present application and the method proposed by Scheele clearly relate to distinct processes.

In sum, Scheele describes proposals that are physiologically incapable of producing the desired effect of treating chronic obstructive pulmonary disease, comprising, among other things, administering at least one osmotically active compound to an airway surface in an amount effective to increase the volume of liquid on the airway surface as recited in claim 1 of the present application. Thus, when considering Scheele in its **totality** for the disclosure that Scheele provides, it is noted that Scheele fails to provide the claim recitations of the present application and fails to provide an enabling disclosure to arrive at the present invention.

Accordingly, Applicant respectfully submits that claims 1, 15, 31-36, 42-44, and 50-51 are not unpatentable under 35 U.S.C. § 102(e) as being anticipated by Scheele and respectfully requests that this rejection be withdrawn.

III. Claim Rejections Under 35 U.S.C. § 103

Claims 1, 14, 15, 20, 31-44, and 50-51 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Scheele in view of U.S. Patent No. 5,162,348 to Glass (Glass) for the reasons set forth in the November Action. More specifically, the November Action asserts that " it would have been prima facie obvious to a person of ordinary skill in the art, at the time the claimed invention was made, to employ more than one of the known salts disclosed by Scheele in the therapeutical composition, or

treating the patient with a bronchodilator before administering the instant composition." November Action, page 3. Applicant respectfully disagrees with this assertion.

For at least the reasons set forth above, Scheele does not teach or suggest all the claim recitations of the present claims. Moreover, in view of the erroneous teachings of Scheele, there is no motivation to modify or even rely upon the teachings of Scheele. Furthermore, the November Action acknowledges that "Scheele does not teach expressly the employment of combination salts, or the further employment of a bronchodilator in the composition." November Action, page 3. Glass is employed to "teach that bronchodilators are well known to be useful for treating cystic fibrosis." November Action, page 3. However, Glass does not supply **all** the missing recitations directed to a method of treating chronic obstructive pulmonary disease using, among other things, at least one osmotically active compound wherein the at least one osmotically active compound comprises at least one salt to alter the volume of liquid on the airway surface as disclosed by the claims of the present invention.

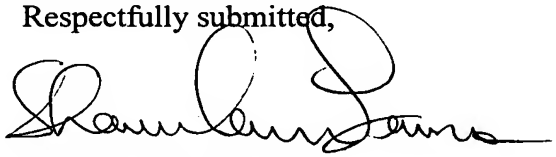
In view of the erroneous teachings of Scheele, either alone or in combination with Glass, Scheele fails to disclose all the claim recitations of the present invention, fails to suggest the modification of the references or the combination of reference teachings in order to arrive at the claimed invention and lastly, fails to provide a reasonable expectation of success.

Accordingly, Applicant respectfully submits that Claim 1, 14, 15, 20, 31-44, and 50-51 are not unpatentable under 35 U.S.C. § 103(a) in view of Scheele in further view of U.S. Patent No. 5,162, 348 to Glass and respectfully requests that this rejection be withdrawn.

Conclusion

In view of the foregoing remarks, Applicant respectfully requests that all outstanding rejections to the claims be withdrawn and that a Notice of Allowance be issued in due course. Any questions that the Examiner may have should be directed to the undersigned, who may be reached at (919) 854-1400.

Respectfully submitted,



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Enclosure: McShane et al., Airway surface pH in subjects with cystic fibrosis. *Eur. Respir. J.* **21(1):**37-42 (2003).

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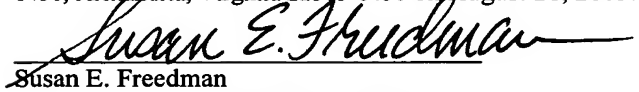

Susan E. Freedman
Date of Signature: August 21, 2003